Remarks

Claims 2-6 and 8-42 are pending. Claims 5 and 8-41 are withdrawn. Claims 2 and 4 are amended. Withdrawn claims that were previously amended are identified as Withdrawn. Claim 1 was canceled in the previous response. Therefore the current rejections of claim 1 are moot. Applicants believe the Examiner intended to apply the rejections of claim 1 to claim 2, and Applicants will respond accordingly.

Rejection Under 35 U.S.C. § 112, first paragraph, written description

Claims 1-4, 6 and 42 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection as it applies to the amended claims.

The Examiner has rejected the claims for lack of written description because claim 2 allegedly encompasses a range of amino acids not explicitly described in the specification. Page 7, line 21 of the specification explicitly recites that the claimed peptide may have about 8, about 9, about 10, about 11, about 12, or about 15 amino acids. Applicants have amended the claim to recite about 9 to 12 amino acids. Accordingly, the rejection should be withdrawn.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 1-4, 6 and 42 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection as it applies to the claims as amended.

The Examiner has rejected claim 2 because it is allegedly unclear where and how many amino acid substitutions occur. Applicants have amended the claim to read "an amino acid substitution at position 2, 9 or both", and therefore, the rejection is now moot.

The Examiner rejected claim 4 as allegedly unclear. Applicants respectfully submit that the one of skill in the art would recognize the meaning of the claim. A plain reading of the claims indicates that the CTL recognizes a cell expressing a polypeptide comprising the HLA-binding peptide of human CD45 polypeptide. Applicant respectfully requests the rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

Claims 1-4 and 6 were rejected under 35 U.S.C. § 103(a) as obvious over International Application WO 97/26328 by RPMS Technology Limited ("WO 97/26328"), in combination with the Leukocyte Antigen Fact Book (2nd Edition, pages 244-247)("Leukocyte") and Rammensee, et al., MHC Ligands and Peptide Motifs, pp 217-227 and 236-281, LANDES Bioscience (1997) ("Rammensee"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Legal Standard

The U.S. Patent and Trademark Office has the burden under 35 U.S.C. § 103 to establish a *prima facie* case of obviousness. *In re Warner et al.*, 379 F.2d 1011, 154 U.S.P.Q. 173, 177 (C.C.P.A. 1967); *In re Fine,* 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598-99 (Fed. Cir. 1988). **To establish a *prima facie* case of obviousness, three basic criteria must be met.** First, there must be some suggestion or motivation, either in the references themselves or in the knowledge

generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck,* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The prior art must provide one of ordinary skill in the art with the motivation to make the proposed modifications needed to arrive at the claimed invention. *In re Geiger*, 815 F.2d 686, 2 U.S.P.Q.2d 1276 (Fed. Cir. 1987); *In re Lalu and Foulletier*, 747 F.2d 703, 705, 223 U.S.P.Q. 1257, 1258 (Fed. Cir. 1984). Claims for an invention are not *prima facie* obvious if the primary references do not suggest all elements of the claimed invention and the prior art does not suggest the modifications that would bring the primary references into conformity with the application claims. *In re Fritch*, 23 U.S.P.Q.2d, 1780 (Fed. Cir. 1992); *In re Laskowski*, 871 F.2d 115 (Fed. Cir. 1989). This is not possible when the claimed invention achieves more than what any or all of the prior art references allegedly suggest, expressly or by reasonable implication.

It is clear that to establish a rejection under 35 U.S.C. § 103 the cited references must (1) recite each element of the claims, (2) provide one of skill in the art with the motivation to combine the cited references and (3) provide one of ordinary skill in the art with a reasonable expectation of success. The references cited by the Examiner clearly do not meet all three criteria.

The Prior Art

WO 97/26328

WO 97/26328 discloses a method for generating cytotoxic T lymphocytes (CTL) against selected peptides presented by a patient's HLA class I molecules. WO 97/26328 states that the peptides must be presented abnormally or must be elevated in diseased cells.

Rammensee

Rammensee discloses residue motifs for peptides that bind to individual class I HLA molecules.

Leukocyte

Leukocyte discloses the amino acid sequence of human CD45.

(1) The cited references must recite each and every element of the claims.

None of these references, alone or in combination, disclose or suggest a peptide of 9 to 12 amino acid residues, wherein the peptide contains the amino acid sequence FLYDVIAST (SEQ ID NO:1) or a variant of SEQ ID NO:1. Therefore, the claims of the present application are not disclosed by nor obvious in view of the cited references.

(2) Provide one of skill in the art with the motivation to combine the cited references.

None of these references provide one of ordinary skill in the art with the motivation to combine these references. None of the references suggest deriving peptides of CD45. WO 97/26328 discloses at pages 7-8 a large list of disease-associated proteins that are suitable targets for tumor immunotherapy. This list does not include CD45. Leukocyte does not disclose or suggest generating peptides of CD45 for immunotherapy. Therefore, one of ordinary skill in that

art would not be motivated to combine WO 97/26328 and Leukocyte to identify epitopes of CD45 for immunotherapy. Furthermore, one of ordinary skill in the art would not be motivated to use CD45 as disclosed in Leukocyte in the method disclosed in WO 97/26328 because CD45 is expressed in haematopoietic malignancies at similar levels as normal cells (see at least page 2, lines 18-19 of the present application) and WO 97/26328 discloses that the antigen for the CTL is expressed abnormally. Since one of ordinary skill in the art would not combine WO 97/26328 and Leukocyte, they would not combine these references further with Rammensee. Therefore, the claims are not obvious over the cited references.

(3) Provide one of ordinary skill in the art with a reasonable expectation of success

The Examiner has not established a *prima facie* case of obviousness. The Examiner has not cited a single place in WO 07/26328, Leukocyte or Rammensee that provides one of ordinary skill in the art with a reasonable expectation of success.

As discussed above, one of ordinary skill in the art would not expect the CD45 of Leukocyte to work in the method of WO 97/26328 because as described in the present application CD45 is expressed in haematopoietic malignancies at similar levels as normal cells. Rammensee discusses principles that were allegedly useful to predict peptides that bind MHC molecules. However, binding **predictions** do not always predict actual binding affinity. There is no way of knowing based on Rammensee whether any CD45 peptides generated through their method would **actually** bind an HLA molecule. The principles disclosed in Rammensee are provided on the internet at

http://www.syfpeithi.de/Scripts/MHCServer.dll/EpitopePrediction.htm (previously filed with

Amendment and Response filed November 21, 2005). Applicants inserted the human sequence of CD45 into the program and searched for peptides of 10 residues in length that bind HLA-0201. The results included a list of **hundreds** of peptides. There is no guidance as to which peptides would actually bind MHC molecules. Without additional guidance, one of skill in the art would have to test each of the peptides to determine which peptides actually bind MHC molecules. In contrast to the unknown properties of Rammensee, Applicants have demonstrated the binding affinity of CD45 peptides (see at least Figure 1 and Example 1).

Rammensee does not provide a reasonable expectation of success for peptides with binding affinity that are also immunogenic (i.e., able to stimulate a CTL response). Based on Rammensee there is no way of knowing whether any of the peptides predicted by Rammensee actually bind the HLA molecule and can stimulate a CTL response. Again in contrast to the cited references, the Applicants have demonstrated immunogenicity of CD45 peptides using allogeneic CTL (see at least Figure 2 and Example 2). This was not predicted but determined experimentally. The cited references also do not provide a reasonable expectation of success for peptides that stimulate CTL to kill tumor cells expressing CD45. Based on the cited references there is no way of knowing which peptides bind the HLA molecule and which actually stimulate a CTL response that would be effective in killing tumor cells that express CD45. Yet again, in contrast to the lack of guidance provided in the cited references, the Applicants have demonstrated that isolated CTLs stimulated by CD45 peptides can kill CD45 expressing tumor cells (see at least Figures 4 and 5). Therefore, the cited references do not provide one of ordinary

skill in the art with a reasonable expectation of success for peptides of CD45. From the forgoing discussion, it is clear that the claims, as amended, are not obvious over the cited art.

Applicants note that the Final Office Action on page 6, item (8) suggests that Fikes et al. (US Patent No. 6,602,510) is being argued separately by Applicant and is not of record in the instant rejection. Therefore, Applicant assumes that any rejection over Fikes is withdrawn.

Allowance of claims 2-6 and 8-42, as amended, is respectfully solicited.

Respectfully submitted,

/Patrea L. Pabst/
Patrea L. Pabst
Reg. No. 31,284

Date: July 11, 2006

PABST PATENT GROUP LLP
400 Colony Square, Suite 1200
1201 Peachtree Street
Atlanta, Georgia 30361
(404) 879-2151
(404) 879-2160 (Facsimile)